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Familial Idiopathic Myelofibrosis and Multiple Hemangiomas

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Idiopathic myelofibrosis (MF) is a rare disease in childhood. The clinical spectrum is very variable. Familial idiopathic MF has been recorded exceptionally. In previous reports idiopathic MF in childhood has been described in association with congenital anomalies and with chromosome abnormalities, although neither of these features have been reported in a familial context. We report two sisters with idiopathic MF and multiple eruptive hemangiomas. Details of their clinical signs, laboratory findings, and histologic features are described. Am. J. Hematol. 59:175–177, 1998. © 1998 Wiley-Liss, Inc.

Key words: myelofibrosis; familial; childhood; hemangiomas

INTRODUCTION

Idiopathic myelofibrosis (MF) is defined as a chronic myeloproliferative disorder of unknown origin characterized by splenomegaly, extramedullary hematopoiesis, leukoerythroblastosis, tear-drop erythrocytes, and varying degrees of myelofibrosis [1]. It is a rare disease in childhood [2–6] and a familial presentation has been exceptionally described [3,4,6]. We report the cases of two sisters with idiopathic MF and multiple hemangiomas.

CASE REPORTS

Patient 1, the first daughter of nonconsaguineous parents, was born in May 1984. Cesarean section at 36 weeks' gestation was done for podal presentation. Her birth weight was 2,900 g. She was admitted to the hospital at the age of four years because of pallor, weakness, and a purpuric syndrome. Physical examination revealed splenomegaly five cm below the left costal margin and multiple hemangiomas on her face, neck, and trunk. These lesions appeared at two years of age. The family history was unremarkable for any hematologic disease. Her laboratory findings were a hemoglobin level of 10.3 g/dl, leukocyte count of 8.2×10^9/l, and a platelet count of 135×10^9/l. The blood film showed leukoerythroblastosis with marked poikilocytosis, abundant tear-drop erythrocytes, immature myeloid cells and Pelger-Huët cells, and nucleated red cells. Neutrophil alkaline phosphatase score was normal. Immunologic evaluation showed normal values of serum immunoglobulins, lymphocyte populations, natural killer cell activity, and immune circulant complexes. Secondary causes of myelofibrosis were excluded. Bone marrows were difficult to aspirate. Normal cellularity of the erythroid, myeloid, and megakaryocytic series were observed. Bone marrow biopsies showed a moderate to severe myelofibrosis. No cytogenetic abnormalities were observed in several analyses during her evolution. Biopsies of two angiomas, done in an interval time of five years, exhibited histologic features of capillary hemangioma. She has experienced recurrent pneumonias upper lobe of the right lung. A computed tomographic scan of the chest showed upper-lobe bronchiectasis. No microorganisms were detected by bronchoalveolar lavage.

At present she is 13 years old; she has shown a progressive enlargement of the spleen up to 11 cm below the costal margin, and a considerable increase in the number

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Fig. 1. Case 1: Multiple hemangiomas on the neck and the back.

of her hemangiomas. Radiologically, apparent sclerosis involving the proximal portion of the long bones and axial skeleton were found. Hematologic laboratory values have remained stable (Fig. 1).

Patient 2, the third child of the parents of patient 1, was born in June 1994, after an uncomplicated pregnancy. An unaffected second brother had been born eight years earlier. The growth and development of Patient 2 were normal. At seven months of age, she was hospitalized because of fever and splenomegaly. Physical examination revealed an otitis and splenomegaly five cm below the left costal margin. Laboratory findings showed a hemoglobin level of 9.6 g/dl, leukocyte count of 25.3×10^9/l, and a platelet count of 93×10^9/l. The blood smear showed myelocytes and nucleated red blood cells together with numerous tear-drop poikilocytes and platelet anisocytosis. Liver and hepatic functions and immunologic evaluation were normal. Secondary causes of myelofibrosis were ruled out. Bone marrow biopsies showed moderate–severe myelofibrosis. No cytogenetic abnormalities were found in two studies.

At the age of two years, three hemangiomas appeared on her forehead and neck. A biopsy confirmed the diagnosis of capillary hemangioma. Now at the age of three, the spleen is enlarged seven cm and the liver two cm below the costal margin. Her hematologic laboratory values have remained stable. HLA (human lymphocyte antigens) typing was performed; no matched familial donor was detected. Both sisters share the same antigens (A2,A31; B44,B51; DR2,DR13).

DISCUSSION

Idiopathic MF is a clonal disease of unknown etiology involving all myeloid elements [7]. Like other myeloproliferative disorders, idiopathic MF rarely occurs in children [2–6]. In reported pediatric cases, idiopathic MF occurs twice as frequently in females as in males [2–6]. A familial presentation of idiopathic MF is extremely rare [4–6].

The clinical course is highly variable. Unlike adult cases of idiopathic MF in children it pursues a more aggressive and invasive evolution [2,3]. Nevertheless, pediatric patients have had a chronic disease with insidious onset and a prolonged course [4–6].

Before making a diagnosis of idiopathic MF in children, a thorough search is needed to exclude secondary causes of bone marrow fibrosis [7]. In one report, idiopathic MF in childhood has been described in association with congenital anomalies [2].

In patients with idiopathic MF, cutaneous manifestations other than those related to hemorrhagic diathesis are uncommon; red cutaneous papulonodules due to skin extramedullary hematopoiesis or tender plaques that resemble Sweet's syndrome have been described [8,9].

Hemangiomas are benign vascular tumors, occurring in up to 10% of infants; approximately one-third of these tumors are capillary hemangiomas. Although various forms of hemangiomas have been related to other clinical syndromes at different ages, no association with idiopathic MF has been reported [10].

The duration of survival in idiopathic MF from diagnosis may vary from less than one year to more than 10 years. Successful bone marrow transplantation has been reported in patients with idiopathic MF and it would be the only potential curative therapeutic possibility [6].

These two sisters were diagnosed with idiopathic MF on the basis of their clinical features, chronic course, hematologic findings, and the histologic appearance of the bone marrow. Both of them also have multiple hemangiomas. In this family, a probable recessive inheritance might be invoked due to the fact that the two affected siblings have parents without signs of idiopathic MF. No suitable familial bone marrow donor was found; a search for an unrelated donor will be done in the case the girls show progressive clinical and hematological deterioration.

In this report, we describe the first reported cases to our knowledge of familial idiopathic MF associated with multiple hemangiomas.

REFERENCES

1. Ward HP, Block MH: The natural history of agnogenic myeloid metaplasia and a critical evaluation of its relationship with the myeloproliferative syndrome. Medicine 50:357–420, 1971.
2. Say B, Berkel I: Idiopathic myelofibrosis in an infant. J Pediatr 64: 580–585, 1964.
3. Boxer LA, Camitta BM, Berenberg W, Fanning JP: Myelofibrosis-Myeloid metaplasia in childhood. Pediatrics 55:861–865, 1975.

4. Sieff CA, Malleson P: Familial myelofibrosis. Arch Dis Child 55:888–893, 1980.
5. Mallouh AA, Rahman SA: Agnogenic myeloid metaplasia in children. Am J Dis Child 146:965–967, 1992.
6. Sekhar M, Prentice HG, Popat U, Anderson D, Janmohammed R, Roberts I, Britt RP: Idiopathic myelofibrosis in children. Br J Haematol 93:394–397, 1996.
7. Weinstein IM: Idiopathic myelofibrosis: Historical review, diagnosis and management. Blood Rev 5:98–104, 1991.
8. Ruberto E, Espinola R, Brusco J, Bacchiocchi M, Zoppi J, Paz R: Mielofibrosis idiopática con focos de hematopoyesis extramedular en piel y testículo. Presentación de un caso. Sangre 40:157–160, 1995.
9. Caughman W, Stern R, Haynes H: Neutrophilic dermatosis in myeloproliferative disorders. Atypical forms of pyoderma gangrenosum and Sweet's syndrome associated with myeloproliferative disorders. J Am Acad Dermatol 9:751–758, 1983.
10. Coffin CM: Vascular tumor. In Pediatric Soft Tissue Tumors. A Clinical, Pathological, and Therapeutic Approach. Baltimore: Williams & Wilkins, 1997.